	VLA-4 (n = 16)	Placebo (n = 15)	P
Lumen (mm^2)	0.18	0.23	0.75
Media (mm^2)	0.21	0.21	0.52
Intima (mm^2)	0.29	0.38	0.30
% Intima	0.59	0.61	0.60

Conclusion: Despite its ability to limit neointimal proliferation in transplant arteriopathy, VLA-4 blockade at the current dose has no significant effect on limiting neointimal proliferation following arterial injury in the rabbit atherosclerotic model.

1039-94 Effect of Latent Cytomegalovirus Infection of Rats on the Neointimal Response to Vascular Balloon Injury

Y.F. Zhou, M. Shou, R.L. Harrell, E.F. Unger, T. Finkel, S.E. Epstein. *National Institutes of Health, Bethesda, MD, USA*

We recently found that prior cytomegalovirus (CMV) infection is a risk factor for restenosis after angioplasty, and *acute* infection of rats with rat CMV (RCMV), 1 day after carotid injury, increases neointimal accumulation. We hypothesized that vascular injury reactivates *latent* CMV; the reactivated virus then exacerbates the neointimal response to injury. Thus, to more critically test the CMV/restenosis hypothesis, we measured the neointimal response to carotid injury following *latent* RCMV infection. Sixty newborn male Sprague-Dawley rats (3 wks old) were randomized into two groups and received an *ip* injection of either 10^6 active RCMV viral particles/ml or saline. Carotid balloon injury was performed 3 mos after infection, when no signs of infection were evident. Rats were sacrificed 6 wks later. Vessels were perfusion-fixed, cut into 3–5 segments, paraffin embedded, and stained by the Movat pentachrome method. The section with the greatest luminal narrowing was planimeterized and normalized by expressing the results as the neointima to media (N/M) ratio. We found that the N/M ratio of rats latently infected with CMV was 41% greater than uninfected controls (mean ± SD: 1.40 ± 0.48 vs 0.99 ± 0.45, respectively; $P = 0.003$). The results were similar when analyzed as % stenosis (44 ± 13% vs 32 ± 14%, respectively; $P = 0.003$). We conclude that CMV has the genetic program that can cause excessive neointimal accumulation in response to vascular injury. The results are also compatible with our hypothesis that arterial injury reactivates latent virus, an event which then leads to cellular processes predisposing to restenosis.

1039-95 Restenosis is Highly Related to Collagen Content and Fiber Organization in the Atherosclerotic Rabbit Model

W.D. Coats, Jr., P. Whittaker[1], D.T. Cheung, J.W. Currier, B. Han, D.P. Faxon. *University of Southern California, Los Angeles, CA, USA,* [1] *>The Heart Institute, The Hospital of the Good Samaritan, Los Angeles, CA, USA*

Prior studies have shown that angioplasty stimulates an increase in both synthesis and degradation of collagen in the atherosclerotic vessel, however, differences in collagen content and metabolism between restenotic (R) and nonrestenotic (N) vessels have not been examined. Accordingly, collagen content in 11 R and N vessels was measured four weeks after angioplasty in an atherosclerotic rabbit model both biochemically by hydroxyproline (OH-pro) quantitation and histologically by a digital subtraction method using circularly polarized images of 20 picrosirius red stained sections. Qualitative and quantitative histologic analysis of collagen fiber organization (CFO) was also performed. Collagenase and gelatinase activities were measured in the same R and N vessels using a radiosubstrate assay. Collagen content was found to be lower in R vs N vessels.

Collagen Content	R	N	p	n
Biochemically (μg OH-pro/mg tissue)	127.0 ± 32.6	212.6 ± 84.3	< 0.05	11
Histologically (% intimal + medial area)	67.3 ± 7.9	76.3 ± 11.8	= 0.05	20

CFO in R vessels was less coherent with loose, more radially aligned fibers vs compacted, more circumferentially aligned fibers in N vessels. In N vessels, 80% of collagen fibers were < 20º from tangential at the point of measurement vs 54% in R vessels ($p = 0.011$; n = 50 fibers). There was a correlation between lumen area and percent collagen content ($p = 0.0071$) and an inverse correlation between collagen content and gelatinase activity ($p = 0.02$). Thus, restenosis is highly related to collagen content and CFO which may be due to increased gelatinase activity.

1039-96 Endoluminal Versus Periadventitial Delivery of Antifibronectin Antibodies. Implications for Local Arterial Wall Delivery

J.-E. Fabre, J.-L. Samuel, L.J. Feldman, L. Rappaport, P.G. Steg. *Faculté Bichat & INSERM U127, Paris, France*

Periadventitial route has been suggested for drug delivery to the arterial wall. Its ability to achieve effective delivery of antibodies (Ab) to the media and intima is unknown. Total fibronectin (FNt) is expressed in rat arterial adventitia and intima. We compared endoluminal vs periadventitial delivery of rabbit polyclonal (IgG) FNt Ab, diluted at 1/20 either in PBS or in pluronic F127 (25% w/v). In 21 Sprague-Dawley rats, the left common carotid artery was exposed. In 8, the pluronic solution containing the Ab was applied onto the arterial adventitia and gelled instantly. In 13 other rats, endoluminal delivery was performed via a dwell method for 30 min. One day later, arterial cryosections were incubated with fluorescent (Texas red) Ab against rabbit to localise the FNt Ab. Controls included arteries either untreated or receiving non specific Ab. Periadventitial delivery via the pluronic gel resulted in labeling of the outer adventitia, but not of the media. The pattern was unmodified by periadventitial polyethylene wrapping or even adventitial stripping prior to delivery. Conversely, endoluminal delivery resulted in consistent labeling of the whole media, up to and including the adventitia. Kinetic studies (5, 15 min, 1, 3, 4 h) demonstrated progressive labeling of the media from the inner to its outer layers within 4 h. *Conclusion:* endoluminal delivery is the route of choice for Ab delivery to the arterial wall, achieving effective intimal, medial and adventitial delivery within 24 h. Conversely, periadventitial delivering of Ab do not allow medial penetration, whereas the endoluminal delivery appear to be the route of choice for specific Ab delivery to the media.

1039-97 Upregulated Arterial Expression of the Estrogen Receptor After Balloon Injury: Role in TGF-β Mediated Repair?

C. Hoffert, M. Labinaz, M.R. Garvin, K. Pels, E.R. O'Brien. *Univ. Ottawa Heart Instit., Ottawa, Canada*

Estrogens act through a specific receptor (ER), and are known to increase TGF-β expression. In human atherosclerosis and restenosis we previously documented the expression of βig-h3, a TGF-β inducible gene that may serve as a biological marker of TGF-β activity. *Purpose:* Determine the arterial expression patterns of the ER and βig-h3 after coronary artery angioplasty. Porcine coronary arteries were harvested 3, 7, 14 and 28 days after angioplasty [balloon:artery = 1.5:1.0; single injury (SI): n = 6; double injury (DI): n = 6]. Six control arteries were also studied. Proliferation, as assessed by incorporation of BrDU, was most pronounced (1–4% of cells) in all arterial layers on day 3 after SI and DI, and primarily involved adventitial and intimal smooth muscle cells (SMCs) and endothelial cells (ECs) of adventitial neovessels. By day 28 after DI adventitial SMCs appeared to migrate inward. Using two independent antibodies, ERs were immunolocalized to the nuclei of a few adventitial cells in normal arteries. In contrast, adventitial > medial > intimal SMCs over-expressed ERs with both cytoplasmic and nuclear distribution patterns early > late after SI and DI. Compared to normal arteries, βig-h3 mRNA and protein were also over-expressed in adventitial SMC and EC early > late after SI and DI. *Conclusions:* Early after injury arterial expression of the ER is upregulated and is associated with the expression of a TGF-β inducible gene. The significance of ER expression in the artery wall is currently being studied, as it may enhance TGF-β expression and therefore, the role of this growth factor in vascular repair.

1039-98 Local Infusion of Vascular Endothelial Growth Factor Following Coronary Angioplasty in Swine

G. Gershony, M. Smyrl, J.M. Brock, N. Ferrara, J.S. Powell. *University of California, Davis, Sacramento, CA, USA*

The major limitation of PTCA is restenosis due to neointimal proliferation and vascular remodeling which is believed to be the result of endothelial denudation and medial injury occurring at the time of angioplasty. To investigate the hypothesis that accelerated reendothelialization would limit the proliferative response to vascular injury, we initiated experiments in pigs to locally infuse the endothelial-specific mitogen, Vascular Endothelial Growth Factor (V), following PTCA. LAD coronary arteries in 28 domestic pigs (weight 38.7 ± 5.6 kg) were subjected to PTCA (balloon/artery ratio 1.3:1) followed by infusion of saline in 15 animals or 0.5 mg of V in 13 animals for 30 min via a local drug delivery catheter (Dispatch™). All animals receiving V experienced significant systemic effects. The systolic blood pressure decreased by 33.7 ± 8.0 mm Hg within 5 min of initiating the V infusion requiring the use of pressors vs 6.8 ± 4.9 mm Hg for the controls ($p < 0.0001$). The P_{O_2} decreased by 165.6 ± 74.7 and 49.2 ± 44.7 mm Hg for the V and control groups respectively ($p < 0.002$). These systemic effects resolved within minutes of stopping the